



## Lateralized modulation of posterior alpha oscillations in children



Madelon A. Vollebregt<sup>a,b,\*</sup>, Johanna M. Zumer<sup>a,1</sup>, Niels ter Huurne<sup>a,b</sup>, Jesminne Castricum<sup>c</sup>, Jan K. Buitelaar<sup>a,b</sup>, Ole Jensen<sup>a</sup>

<sup>a</sup> Centre for Cognitive Neuroimaging, Donders Institute for Brain, Cognition and Behaviour, Radboud University, Kapittelweg 29, 6525 EN Nijmegen, Netherlands

<sup>b</sup> Karakter Child and Adolescent Psychiatry University Centre, Reinier Postlaan 12, 6526 GC Nijmegen, Netherlands

<sup>c</sup> Center for Neuroscience, Swammerdam Institute for Life Sciences, Faculty of Science, University of Amsterdam, 1090 GB Amsterdam, The Netherlands

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### ABSTRACT

The evidence for a functionally inhibitory role of alpha oscillations is growing stronger, mostly derived from studies in healthy adults investigating spatial attention. It remains unexplored if the modulation of alpha band oscillations plays a similar functional role in typically developing children. The aim of this study was to characterize alpha modulations in children in relation to attentional performance. To this end, the posterior alpha activity (8–12 Hz) in children between 7 and 10 years old was measured using EEG while they performed a visuospatial covert attention task. We found that the alpha activity decreased in the hemisphere contralateral to the attended hemifield, whereas it relatively increased in the other hemisphere. In addition, we found that the degree of lateralized alpha modulation predicted performance on the attention task by negatively predicting the response time on invalid trials. Of note, children who were behaviorally less influenced by spatial cueing also were children with a clear lateralized alpha modulation pattern, with a significantly stronger alpha lateralization in the left hemisphere than children who were influenced more by spatial cueing. In addition, a bias to the right visual field such as that commonly observed in children, was significantly smaller or absent in the children influenced least by spatial cueing. Among all children, the magnitude of this visual field bias was positively related to the ability to modulate alpha activity. In conclusion, we have shown that the pattern of alpha oscillations modulated by attention is already present in 7–10 year old typically developing children. Although a similar pattern is observed in adults, the consequences for behavior are different. The fact that alpha modulation is already present at this age opens up the possibility of using hemispheric alpha lateralization as a tool to study the physiological basis of attention deficits in clinical disorders such as ADHD.

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### Introduction

Allocation of attention requires a focus on relevant and simultaneous suppression of irrelevant information (Posner and Petersen, 1990). Increasing evidence has demonstrated that allocating spatial attention is associated with regional specific modulation of alpha oscillations (8–12 Hz). These oscillations have been suggested to gate streams of information through the brain network by means of functional inhibition (Klimesch et al., 2007; Thut and Miniussi, 2009; Snyder and Foxe, 2010), a process described by the ‘alpha inhibition hypothesis’ (Jensen and Mazaheri, 2010). The functional role of alpha activity in healthy adults has particularly been studied using visuospatial covert attention

cueing paradigms based on variations of Posner’s paradigm (Posner, 1980). In most electroencephalography (EEG) and magnetoencephalography (MEG) investigations of covert spatial attention, a cue directs attention to the left or right visual hemifield, which allows for investigating the alpha power in the hemispheres processing the attended and unattended visual hemifields. The key finding has been that posterior alpha power increases ipsilateral and decreases contralateral to the attended visual hemifield, respectively inhibiting or facilitating the information flow (Worden et al., 2000; Sauseng et al., 2005; Kelly et al., 2006; Thut et al., 2006; Händel et al., 2011; Bengson et al., 2012; ter Huurne et al., 2013). High alpha power over task-irrelevant regions linked to the processing of the unattended information, has proved to be of crucial importance for optimal attentional performance (Romei et al., 2010; Händel et al., 2011). Whether similar modulations of posterior alpha power can be observed in children is not known yet.

While rudimentary forms of attentional functions are already present at birth and further develop during the very first year of life (Colombo, 2001), the ability to allocate attention keeps developing throughout childhood (Rueda, 2013). For instance, orienting of attention seems to improve from 6 or 7 years onwards by gaining the ability

\* Corresponding author at: Donders Institute for Brain, Cognition and Behaviour, Donders Centre for Cognitive Neuroimaging, Kapittelweg 29, 6525 EN Nijmegen.

E-mail addresses: [m.vollebregt@donders.ru.nl](mailto:m.vollebregt@donders.ru.nl) (M.A. Vollebregt),

[johanna.zumer@gmail.com](mailto:johanna.zumer@gmail.com) (J.M. Zumer), [n.terhuurne@karakter.com](mailto:n.terhuurne@karakter.com) (N. ter Huurne),

[jesminne@gmail.com](mailto:jesminne@gmail.com) (J. Castricum), [jan.buitelaar@radboudumc.nl](mailto:jan.buitelaar@radboudumc.nl) (J.K. Buitelaar),

[o.jensen@donders.ru.nl](mailto:o.jensen@donders.ru.nl) (O. Jensen).

<sup>1</sup> Present address: School of Psychology and Centre for Computational Neuroscience and Cognitive Robotics, University of Birmingham, B15 2TT, UK.

to disengage attention when necessary (Schul et al., 2003; Wainwright and Bryson, 2005). The fully developed attentional network has been proposed to involve two main systems: 1) a largely bilateral dorsal fronto-parietal system that is involved in goal-directed stimulus-response selection, and 2) a right-lateralized ventral system, that directs the attention to salient unexpected stimuli. The ventral system is thought to work as an alerting mechanism engaging the dorsal system when unexpected stimuli are detected (Corbetta and Shulman, 2002). We propose that in Posner's cueing paradigm, the dorsal system enables early orienting towards a cued location and the ventral system is required for shifting attention towards 'surprise' targets in the uncued hemifield. According to the alpha inhibition hypothesis, we would be able to measure lateralized alpha modulation during the preparation interval, when goal-directed allocation of attention is expected.

It is unclear whether children display lateralized posterior alpha modulation with spatial attention similar to adults and whether changes in alpha power relate to behavioral performance. The aim of this study was to investigate how alpha modulations observed in children relate to previous observations in adults. To this end, we investigated the modulation of oscillatory brain activity as recorded by EEG in relation to behavioral performance of 7 to 10 year old typically developing children performing a visuospatial covert attention task.

## Materials and methods

### Participants

Data were acquired in the context of a clinical trial investigating alpha oscillations in children with and without ADHD (ClinicalTrials.gov identifier NCT01932398). The study was approved by the local Medical Ethics Committee (<http://www.cmoregio-a-n.nl/>) and conducted in accordance with the Declaration of Helsinki. All parents gave written informed consent, children gave oral assent. Here we reported information relevant to the present study only, focusing on typically developing children, i.e. not the children with ADHD.

Children in the age range from 7 to 10 years old were recruited from primary schools in the area of Nijmegen, the Netherlands. Children were included if they never had a psychiatric, neurological, or cardiovascular disease or serious motor or perceptual handicap; and if their estimated IQ was above 80. If an intelligence test had not taken place over the past two years, two subtests (i.e. Vocabulary and Block Design) of the Wechsler Intelligence Scale for Children (WISC-III; Wechsler, 1991; Dutch version: de Kort et al., 2002) were administered to estimate the intelligence. The Child Behavior Checklist (CBCL; Verhulst et al., 1996) was used to rule out the presence of clinical behavior. Data were collected between April 2012 and June 2014. Parents received reimbursement for travel costs and children received a present.

Twenty-seven right-handed children were included in this study. Data from three children were excluded ( $N = 2$  technical problems,  $N = 1$  task performance below chance level). Three other children were identified to have very few correct responses on the invalid trials ( $10.2 \pm 15.9\%$ ). Data from these children were rejected for further analyses because 1) it was not possible to calculate behavioral performance on invalid trials and the subsequently derived cueing effect based on response time (RT) for these children since RTs for invalid trials were lacking, 2) these children responded significantly faster ( $N = 3$ :  $262.61 \pm 31.14$  ms) on the available valid trials than the other children ( $N = 20$ :  $571.22 \pm 104.59$  ms) ( $t(21) = 4.987$ ,  $p < .001$ ), suggesting they used a different strategy. Final analyses were therefore conducted using data of the remaining 21 children (mean age,  $9.11 \pm 1.29$ ; 42.9% boys; estimated IQ,  $119.23 \pm 17.63$ ).

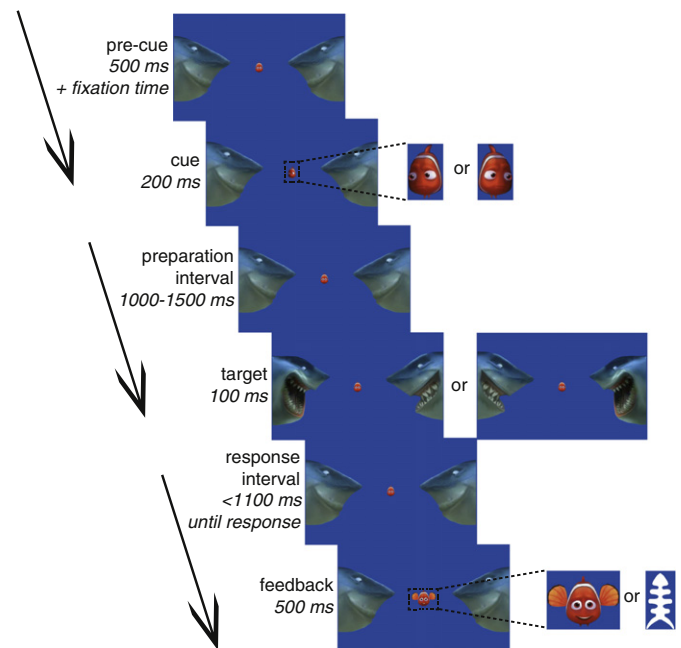
### Study procedure

All measurements were performed at the Donders Centre for Cognitive Neuroimaging, Nijmegen, the Netherlands. Children and their

parents visited the institute twice. First, if not available, intelligence was estimated. Furthermore, the first visit was used to explain and practice the visuospatial covert attention task, subsequently referred to as *the attention task*. This practice session was conducted while tracking the eyes to train the children to keep fixated at the center, but without EEG measurement. During the second visit the attention task was performed while tracking the eyes and recording the EEG. In addition, two resting state EEG sessions, in which the child was instructed to sit quietly for 2 min with eyes open and 2 min with eyes closed, were recorded during the second visit. Analyses of these data are not presented here.

### The attention task

An adjusted version of Posner's cueing paradigm for spatial orienting of attention was used (Posner, 1980), in which the goal was to save a fish from being eaten by a shark (Fig. 1). The task was programmed and presented using the software package Presentation (Neurobehavioral Systems, Albany, CA). The task started with a 1 min introduction video in which a shark recapped the most important instructions. Trials started with a pre-cue period (500 ms) with a shark presented at each side of the screen and a fish presented centrally. The child viewed the screen from a 50 cm distance creating an angle of 5.5 degrees with the innermost edge of the target figures. Note that the most informative part of the target was between the edge (5.5 degrees) and the middle of the target figures (13.1 degrees). The child was instructed to fixate at the fish in the middle of the screen and to sit as quietly as possible throughout the task. Influences of movement on the eye tracker and EEG recordings were shown to the child in advance to illustrate the importance of sitting still. An attentional cue was presented in a 200 ms interval, in which the fish shifted gaze towards the left or the right shark indicating the side of the upcoming target if validly cued or indicating the opposite side if invalidly cued. In the next period (1000–1500 ms



**Fig. 1.** The attention task. After a neutral pre-cue period in which a fish and two sharks were presented on the screen, children were cued to attend to the left or the right visual hemifield while keeping fixation at the centrally presented fish. After a 1000–1500 ms preparation interval, both sharks opened their mouths; one more so than the other. Children had to report which shark had the widest opened mouth. In 75% of the trials the widest opened mouth was in the cued visual hemifield (*valid cue trial*), whereas in 25% surprise trials the mouth was widest opened in the other hemifield (*invalid cue trial*). Following a correct response within the response interval, a happy fish was presented. For incorrect responses, the fish was replaced by a fishbone.

jittered) the child was expected to prepare for the upcoming target, hence this period was referred to as the *preparation period*. Next, the sharks both opened their mouths (100 ms), the target being the shark with the widest mouth. The child had to press the left or right button with the right index or middle finger to indicate the left or right shark, respectively. Correct responses had to be delivered within 1400 ms after target presentation to prevent negative feedback. Depending on the button press, positive or negative feedback was then presented for 500 ms, consisting of a happy fish or a fish bone, respectively. As encouragement a short task-related video with a shark was shown after every 37 trials.

During the first visit, the child practiced 100 trials (40 valid trials and 10 invalid trials per visual hemifield). Hence, the cue predicted the target location in 80% of the trials. During the second visit, the task consisted of 368 trials (138 valid trials and 46 invalid trials per visual hemifield). Hence, the cue predicted the target location in 75% of the trials. The correct prediction of the cue was set higher in the practice session to stimulate the child to use the cue information while learning the task. The left or right cue occurred with equal probability.

### Eye tracking

Eye gaze was calibrated using a corneal reflection eye tracker and ClearView software (Tobii 1750, Tobii Technology Sweden), recording both eyes. Following a five point calibration procedure, the eye tracker made it possible to monitor fixation during the pre-cue and preparation period. During the pre-cue period, the cue was presented only when the child fixated on the screen center. If not fixating during the subsequent preparation period, three different types of instruction videos were presented immediately depending on the size of the deviation from the middle. It gave instruction to fixate on the eyes of the fish (small deviations), to fixate on the fish (median deviations), or to not look at the sharks (large deviations).

### EEG recordings

The EEG was recorded continuously during a 2 min eyes-open and a 2 min eyes-closed resting-state condition, and during the attention task. It was recorded from 32 scalp electrodes placed according to the 10–20 system using the actiCAP and BrainAmp system (Brain Products GmbH, Munich). The vertex (electrode between Cz and Fz) was used as online reference; offline the data were referenced to the average of all electrodes. Electrode Fpz was used as ground. Electrode impedance was kept below 20 kOhm. The data were sampled at 500 Hz following a 0.016 Hz high-pass and a 125 Hz lowpass filter. The gain was set to 0.1  $\mu$ V resolution per bit.

### Analyses

Data were processed and analyzed using MATLAB 2012a (The MathWorks, Inc., Natick, MA) and the FieldTrip analysis toolbox (<http://fieldtrip.fcdonders.nl>). When correlation analyses were performed, these were always tested non-parametrically using a Spearman correlation test.

### Behavioral performance

RTs were expected to be distributed as an exponentially modified Gaussian (ex-Gaussian) distribution, implying that RTs contained a mean ( $\mu$ ) and standard deviation ( $\sigma$ ) of a Gaussian component and a mean ( $\tau$ ) of the exponential component (Lacouture and Cousineau, 2008). We expected that cueing effects would be reflected by changes in mean of the Gaussian component rather than in the exponential component of the ex-Gaussian distribution. Therefore, all RT analyses were conducted using the  $\mu$  of RT ex-Gaussian distribution. Furthermore, RTs faster than 100 ms were considered too short to reflect stimulus perception (Luce, 1986), while RTs larger than 4 times

the standard deviation of the mean were regarded outliers (Schmiedek et al., 2007). These trials were therefore rejected from behavioral analyses.

### Spectral analysis of the EEG data

Data segments showing artifacts such as muscle potentials, and amplifier or electrode noise, were identified using a semiautomatic routine and excluded from further analyses. An independent component analysis was used to detect and remove component(s) with electrooculographic origin, using a *fastica* algorithm (Hyvärinen, 1999). The EEG recordings were bandpass filtered at 2–30 Hz. Only trials in which the child fixated were used for further analysis. Fast Fourier Transform, with a time-window of  $T = 5$  cycles ( $T = 5/f$ ) and a Hanning taper, was used to calculate time-frequency representations of power (2–30 Hz, with a frequency resolution of 2 Hz). The time interval was either cue-locked from  $-0.25$  to 1.5 s around cue-onset or target-locked from  $-1$  to 0.2 s around target-onset. The alpha modulation index (MI) from cue-locked data was used to investigate whether a task-based modulation could be observed in the alpha band (8–12 Hz). The MI was computed by subtracting alpha power of right-cued trials from left-cued trials for each electrode. This subtraction was subsequently normalized by dividing by half of the sum of these values:

$$MI = \frac{(\alpha_{\text{left cued trials}} - \alpha_{\text{right cued trials}})}{\frac{1}{2} (\alpha_{\text{left cued trials}} + \alpha_{\text{right cued trials}})}$$

The MI was averaged over left (left MI) and right (right MI) hemisphere parietal and occipital electrodes (left: P3, PO9, O1; right: P4, PO10, O2). From these values we constructed a combined MI (left MI minus right MI).

A cluster based permutation test was performed to identify time clusters for which the left MI differed significantly from right MI (van Ede et al., 2011). This test controls multiple comparisons by identifying significant clusters of time points rather than significant individual time points over the time-interval ( $-0.2$  to 1.5 s). The longest significant time cluster was used for further analyses. Similar analyses were conducted for target-locked data (time interval  $-1$  to 0.2 s).

## Results

The visuospatial covert attention task performed by the 21 children is shown in Fig. 1. The fish in the middle cued the children to attend to the left or the right shark. After a preparation interval (1000–1500 ms), both sharks opened their mouth and the children had to indicate with a button press which of the two sharks opened their mouth the widest. In 75% of the trials, the cued shark did.

### Behavioral performance

All children completed the task consisting of 368 trials. After rejection of trials where fixation was lost and trials containing artifacts,  $176 \pm 29$  trials remained for EEG-analyses. Of these, in  $44 \pm 8$  trials the target was invalidly cued. The RT distributions were fitted to an ex-Gaussian distribution (for example, see supplementary material Fig. A.1). All further analyses were therefore conducted using  $\mu$ , which represents the mean of the RTs when controlling for the exponential component of the distribution. As expected, children responded faster to validly cued targets ( $461 \pm 94$  ms) than invalidly cued targets ( $517 \pm 103$  ms) resulting in a statistically significant cueing effect (paired  $t$  test,  $t(20) = -6.98, p < .001$ ). The cueing effect was also observed when considering hit-rates; children were significantly more accurate on validly cued targets ( $94.34 \pm 7.79\%$ ) than invalidly cued targets ( $90.99 \pm 12.41\%$ ) ( $t(20) = 2.51, p = .02$ ). The magnitude of the RT cueing effect was not significantly related to age ( $r = .301, p = .186$ ), nor was the hit-rate cueing effect ( $r = -.038, p = .872$ ). Since the cueing effect

was more variable over children when considering RTs, this behavioral measure was chosen for further analyses.

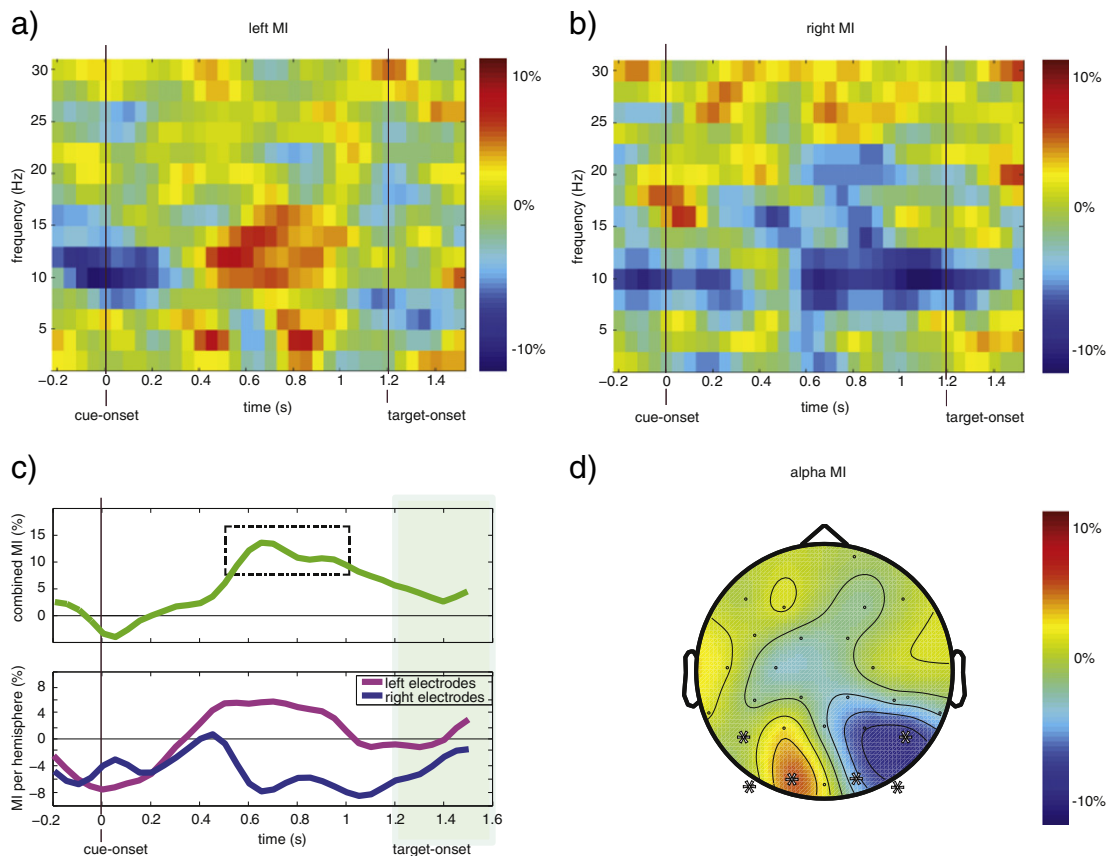
### Modulation in the alpha band

To study hemispheric modulation of oscillations following the cue initiated allocation of attention in children, we contrasted the spectral power for left versus right cues for each hemisphere separately and in combination. Time-frequency representations of power for left cued trials minus right cued trials, normalized by their mean and averaged over left (Fig. 2a) and right (Fig. 2b) occipital and parietal electrodes demonstrated a clear modulation mainly constrained to the alpha band. The alpha power decreased in electrodes contralateral to the cue while it relatively increased in ipsilateral electrodes. Note the modulation observed around the cue-onset (Fig. 2a). This modulation was however not significant ( $t = -0.1$  to  $0.1$  ms interval tested). This was also confirmed when directly comparing left and right electrodes (Fig. 2c, bottom panel). When combining the modulation in the alpha band (8–12 Hz) by subtracting the left and right hemisphere MI (Fig. 2c, top panel), it became clear that the modulation with attention was most pronounced  $\sim 0.6$  s after cue-onset. A permutation test controlling for multiple comparisons over time verified that left and right MI in the alpha band significantly differed from each other and that this difference was most pronounced in the interval 0.50–1.05 s after cue-onset ( $p = .002$ ) (indicated by the dashed square, top panel). Data was then averaged over these time points and the alpha frequency band, and finally over participants, to create a topographic representation (Fig. 2d). We observed

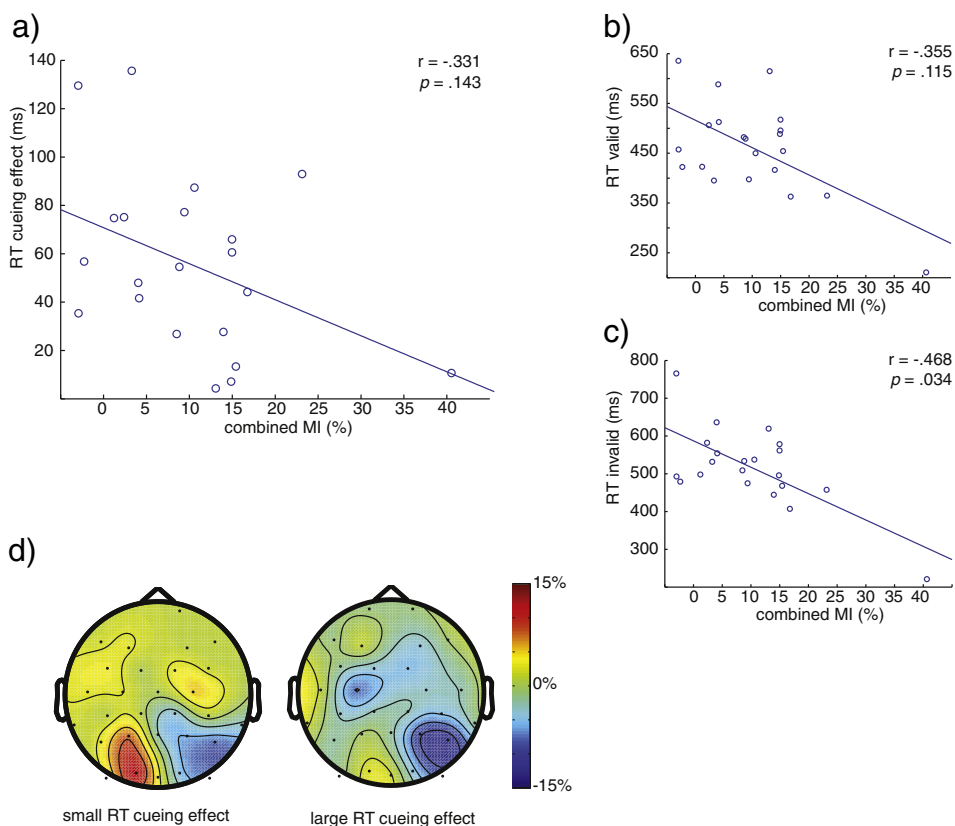
that the modulation in the alpha band was stronger over occipital and parietal electrodes. Similar analyses were performed for data that were time-locked to the target-onset. Visualization of these data is shown in the supplementary material (Fig. A.2). A time cluster permutation test revealed one significant cluster in the period 0.95–0.50 s before target-onset ( $p = .002$ ). This time-window overlapped with the interval identified in the cue-locked data. In short, we have demonstrated that, as in adults, posterior alpha band activity is robustly modulated by spatial attention in children.

### Alpha modulation and behavioral performance

We subsequently asked whether the ability to modulate alpha activity correlated with attentional performance. Hence, we correlated the combined cue-locked MI in the alpha band (0.50–1.05 s) with the RT cueing effect ( $\mu$  for cued compared to uncued targets). Contrary to our expectations, we did not observe a significant correlation ( $r = -.331$ ,  $p = .143$ ). The direction of this relationship was opposite to that found in [ter Huurne et al. \(2013\)](#) (Fig. 3a). Although a relationship between RT on valid trials and combined alpha MI was absent ( $r = -.355$ ,  $p = .115$ ) (Fig. 3b), a faster response to invalid trials was related to stronger MI ( $r = -.468$ ,  $p = .034$ ) (Fig. 3c). The child that seemed to have an atypical response (high MI and fast RT) was not rejected since our criterion for rejecting participants (see Method section) was not applicable. The rejected children described in section 2.1 had  $10.2 \pm 15.9\%$  correct answers on invalid trials, while this particular child had 42.3% correct answers on invalid trials and 68.8% on valid trials.



**Fig. 2.** The modulation of alpha band power in response to the spatial cue. *a.* Time-frequency representation of the MI (normalized modulation in power for left minus right cues) averaged over children in left occipital and parietal electrodes. The alpha power was stronger for left (ipsilateral) compared to right (contralateral) cues. The vertical line at zero represents cue onset. The vertical line at  $t = 1.2$  s represents the first possible target-onset. *b.* Similar to *a*, for right electrodes. The alpha power was weaker for left (contralateral) compared to right (ipsilateral) cues. *c.* (Top panel) Time-course of the combined MI (left electrode MI minus right electrode MI) averaged over children (occipital and parietal electrodes), in the 8–12 Hz alpha band. The dashed square indicates the time cluster for which the MI in left electrodes and right electrodes differed significantly ( $t = 0.50$ – $1.05$  s;  $p = .002$ ) from each other. The vertical line at zero represents cue onset. The green area indicates the jittered possible onsets of the target presentation (last possible onset at 1.7 s). (Bottom panel) Time course of the left MI and right MI separately. *d.* Topographic representation of the MI averaged over children, in the alpha band ( $t = 0.50$ – $1.05$  s). The alpha power that is clearly lateralized with respect to the spatial cue appears restricted to the posterior electrodes. Stars indicate the selected channels for further analyses.



**Fig. 3.** Relating the modulation of alpha power to attentional performance. *a.* The relationship between the combined MI in the alpha band and the RT cueing effect ( $r = -.331, p = .143$ ). The RT cueing effect was defined as the  $\mu$  on invalidly cued trials minus the  $\mu$  on validly cued trials *b* & *c.* The relationship between the combined MI in the alpha band and the RT on (b) valid trials ( $r = -.355, p = .115$ ) and on (c) invalid trials ( $r = -.468, p = .034$ ). *d.* Topographic representations of the MI in the alpha band ( $t = 0.50$ – $1.05$  s) for children with a small and large RT cueing effect.

We further investigated the relationship between alpha MI and attentional performance by separating the children in two groups according to the cueing effect observed in the RTs. We found that in children with a small cueing effect ( $N = 11$ ), the topographic representation of the MI was pronounced (Fig. 3d left), but no clear lateralized modulation was observed in children with a large cueing effect ( $N = 10$ ) (Fig. 3d right). These groups significantly differed from each other with respect to MI in the left hemisphere ( $t(19) = 2.482, p = .023$ ) but not right ( $t(19) = 0.339, p = .738$ ). When considering the target-locked data, we confirmed the absence of a significant correlation between the combined MI in the alpha band and the RT cueing effect ( $r = -.313, p = .167$ ) as well as between combined alpha MI and valid trials RT ( $r = -.304, p = .180$ ). We did not confirm a relationship between  $\mu$  RT on invalid trials and alpha MI ( $r = -.364, p = .106$ ). We conclude that children that modulate the posterior alpha band activity the strongest are children that are influenced least by the spatial cueing, most likely having the least difficulty with an unexpected switch of attention. However, children with a small cueing effect ( $489 \pm 112$  ms) were not significantly faster on invalid trials than children with a large cueing effect ( $547 \pm 89$  ms) ( $t(19) = -1.287, p = .214$ ), nor were they slower on valid trials (small cueing effect group:  $461 \pm 109$  ms, large cueing effect group:  $461 \pm 80$  ms,  $t(19) = 0.000, p = 1.00$ ).

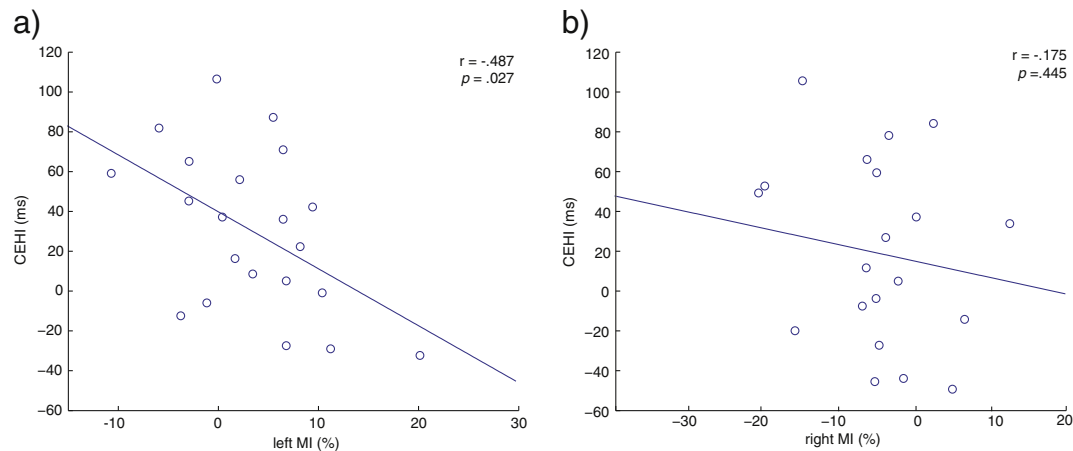
#### The influence of a right visual hemifield bias

Since children are known to display a bias towards the right visual hemifield (Takio et al., 2013) in contrast to adults who display a bias to the left visual hemifield (Bowers and Heilman, 1980; Manly et al., 2005), we investigated the presence of such a bias and its relation to

the ability to modulate alpha activity. In our sample, children were indeed significantly faster ( $t(20) = 2.091, p = .049$ ) on valid trials cued to the right visual hemifield ( $453 \pm 96$  ms) compared to the left visual hemifield ( $468 \pm 94$  ms). This difference was not apparent for the invalid trials ( $t(20) = 0.488, p = .631$ ).

We then created a measure representing the hemifield bias termed the *Cueing Effect Hemifield Index* (CEHI): the right cueing effect versus the left cueing effect, i.e., the cueing effect for right responses minus the cueing effect for left responses. There was a strong trend towards a faster cueing effect in the right hemifield than in the left hemifield ( $t(20) = 2.050, p = .054$ ). Interestingly, when a median split was performed based on RT cueing effect (same groups as Fig. 3d), children who displayed a small cueing effect did not show a significant CEHI ( $t(10) = -0.144, p = .889$ ) while children who displayed a large cueing effect clearly did show a significant CEHI ( $t(9) = 3.267, p = .010$ ). When these groups were compared on CEHI using a two sample *t*-test, a significant difference was found ( $t(19) = 2.64, p = .016$ ); children with a large RT cueing effect had a rightward bias (CEHI:  $43 \pm 13$  ms) while children with a small RT cueing effect had not (CEHI:  $-2 \pm 11$  ms). The CEHI was not significantly correlated with age ( $r = -.118, p = .609$ ).

Next, we queried whether there was a relationship between the alpha MI and the behavioral CEHI. We found no significant correlation between the combined MI in the alpha band and the CEHI ( $r = -.216, p = .346$ ). However, when considering the hemispheres separately, the left electrode MI showed a significant correlation with CEHI ( $r = -.487, p = .027$ ): children with a diminished ability to modulate alpha activity in the left hemisphere displayed a stronger bias to the right visual hemifield. (Fig. 4a). For the right MI, no such correlation was found ( $r = -.175, p = .445$ ) (Fig. 4b).



**Fig. 4.** The alpha modulation index per hemisphere in relation to bias in cueing effect hemifield index. *a.* Relationship between left electrode MI in the alpha band and the right cueing effect minus the left cueing effect. *b.* Similar to *a* but for the right MI.

All in all, we found that a smaller rightward bias was related to a stronger ability to modulate alpha activity in the left hemisphere as well as to making less use of the spatial cueing.

However, rather than predicting the expected cueing benefit, posterior alpha modulation negatively predicted the response time on invalid trials. This finding is a surprise given that studies in adults found, the reverse relation (ter Huurne et al., 2013).

## Discussion

The current study investigated the modulation of alpha band activity in 7–10 year old typically developing children performing a visuospatial covert attention task while EEG was recorded. We found that the alpha power (8–12 Hz) decreased in the hemisphere contralateral to the attended hemifield, whereas it increased relative in the other hemisphere. This pattern was consistent with what studies previously found in adults (Worden et al., 2000; Sauseng et al., 2005; Kelly et al., 2006; Thut et al., 2006; Händel et al., 2011; Bengson et al., 2012). In addition, we found a relationship between the posterior alpha modulation and attentional performance. However, rather than predicting the expected cueing benefit, posterior alpha modulation negatively predicted the response time on invalid trials. This finding is a surprise given that studies in adults found the reverse relation (ter Huurne et al., 2013). Children with a large cueing effect showed significantly less left hemisphere alpha modulation than children with a small cueing effect. Furthermore, children with a large cueing effect were those that displayed a significantly stronger bias to the right visual field. The magnitude of this rightward bias was negatively correlated with left hemisphere alpha modulation. A rightward bias is thought to change as a function of age, being more common in children and elderly than in young adults (Takio et al., 2013). All in all, an increased ability to modulate alpha activity in either or both hemispheres was associated with a smaller cueing effect and a diminished rightward visual bias.

We quantified the relationship between the alpha modulation and behavior for both cue-locked and target-locked behavior. The rationale for examining the target-locked alpha modulation was based on results shown by ter Huurne et al. (2013). This study showed a lack of maintenance of the alpha modulation during the preparation interval in adults with ADHD and also showed a different relationship of alpha lateralization preceding the target to behavioral performance between adults with and without ADHD. Since the healthy children from the current sample showed a bias to the right visual hemifield similar to adults with ADHD (ter Huurne et al., 2013), we additionally investigated alpha activity preceding the target. In general the relationship was stronger in these healthy children for the cue-locked alpha modulation

compared to target-locked. This is partly explained by the target-onset being jittered in time. It also means that the ‘attentional state’ as reflected by the alpha band activity was coordinated by the cue rather than the anticipation of the target.

Although based on previous results in adults we would have expected alpha modulation to be stronger along with the ability to allocate attention, i.e. along with the cueing effect (ter Huurne et al., 2013), we did not find such a relationship. We even found that lateralized alpha modulation was more pronounced in children with a small rather than large cueing effect. One interpretation of these results would be that alpha activity in the posterior brain areas in children is not predictive of inhibition of the visual stimuli, inconsistent with the alpha inhibition hypothesis. Following this interpretation the functionality of alpha activity might change during the course of development. The results might however also be explained from a broader developmental perspective. That is, while developmental improvement of alertness (Berger et al., 2000) and orienting (Schul et al., 2003) may decrease response times of valid cues, the developmental facilitation of attention disengagement may decrease response time following invalid cues even more, hence reduce the difference between invalid and valid trials (Schul et al., 2003). This would mean that a cueing effect decreases with the increased ability to disengage attention, i.e. with development. Since attention disengagement is thought to be related to the stimulus-driven ventral stream while the top-down dorsal system is thought to be most strongly related to goal-driven preparation, alpha modulation – influenced by frontal structures known to be part of the dorsal system (Marshall et al., accepted for publication; Sadaghiani et al., 2010; Zumer et al., 2014) – could be hypothesized to be present independent of the ability to disengage attention. However, the two networks are not thought to work in isolation, but will interact in a flexible manner (Vossel et al., 2014). A smaller cueing effect due to improved attention disengagement in these developmentally crucial years may be somewhat separate from a relationship between alpha modulation and attention allocation. Still, a suboptimal interaction between and/or a slower development of both the dorsal and ventral attention networks might explain a less clear alpha modulation pattern in children with a large cueing effect (i.e. less disengagement of attention). It might also explain the subtle relationship that we found between RT on invalid trials and alpha modulation, since disengagement of attention is needed in response to the invalid trials.

Children with a large cueing effect had a significantly larger bias to the right visual hemifield than children with a small cueing effect. A study that investigated both attention disengagement and biases showed that the youngest children (6 years old) both had attention disengagement problems and showed a bias to the right visual hemifield

whereas both of these effects were reduced in the older children (Wainwright and Bryson, 2005). This might suggest that a developmental shift in attentional bias co-occurs with improvement of attention disengagement. In addition, a significant negative correlation between the rightward bias magnitude and left hemisphere alpha modulation may be in line with the notion that alpha modulation is related to attentional performance. A rightward bias is not only seen in children (Takio et al., 2013), it is also seen in healthy adults after spending a long time on a task (Newman et al., 2013; Manly et al., 2005) as well as in adults with ADHD (ter Huurne et al., 2013). Hence, a right hemifield bias seems to be related to a suboptimal attentional performance. In our study the rightward bias was associated with a low ability to modulate alpha activity in the left hemisphere and a large cueing effect. One explanation is that a left hemisphere alpha power increase is required to shift attention from right to left, and children have reduced ability in doing so.

## Conclusions

In conclusion, we were able to show that the pattern of alpha oscillations modulated by attention is already present in 7–10 year old children. However, its relationship with behavioral performance was somewhat opposite as compared to previous findings in adults. Although this seems counterintuitive at first glance, children of this age range exhibit a range of abilities: those with the least maturation of shifting from a rightward to leftward visual bias also exhibit other, possibly less-developed characteristics, namely a larger cueing effect and reduced left alpha MI. The development of attentional networks, and especially the development of attention disengagement may explain why a smaller effect of cued attention allocation may reflect better attentional performance, hence a stronger modulation of alpha activity. In particular our data suggest that children have an enhanced ability to attend to the right; this seems to be explained by alpha oscillations in the left hemisphere not being strong enough to break the attentional focus. Why is this effect only present for the right and not the left hemifield? Given that the ventral network controlled by structures around the right temporal parietal junction (TPJ) is required for exogenously driven attention switches, we speculate that connections from the right TPJ influencing the left hemisphere alpha oscillations remain to mature in children. The fact that alpha modulation is already present at this age opens up the possibility of using lateralized alpha modulation as a tool to mechanistically study clinical attention deficits such as in children with ADHD.

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## Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Buitelaar has been for the past years a consultant to, member of the advisory board of, and/or speaker for Janssen Cilag BV, Eli Lilly, Bristol-Myers Squibb, Schering-Plough, UCB, Shire, Novartis, and Servier. He is neither an employee of nor a shareholder in any of these companies. He receives no other financial or material support, including

expert testimony, patents, and royalties. The other authors have no conflict of interest to report.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2015.06.054>.

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